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10-Year Diagnostic Consistency of Bipolar Disorder in a First-Admission Sample

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Abstract

Objectives—A number of reports have examined the stability of the diagnosis of schizophrenia, but fewer studies have considered the long-term consistency of a bipolar diagnosis or factors that influence the likelihood of a diagnostic change. The present study sought to estimate how consistently a bipolar diagnosis was made across a 10 year period and factors associated with consistency, particularly demographic and clinical characteristics, childhood-related factors, and illness course.

Methods—The sample included 195 first admission patients presenting with psychosis who were assessed soon after hospitalization and at 6-month, 2-year, and 10-year follow-up and diagnosed with bipolar disorder on at least one of these assessments. Diagnoses were made using best-estimate procedures and were blind to all previous consensus diagnoses. Respondents who were consistently diagnosed with bipolar disorder were compared to those whose diagnosis shifted across assessments.

Results—Overall, 50.3% (n = 98) of the 195 respondents were diagnosed with bipolar disorder at every available assessment, but 49.7% (n = 97) had a diagnostic shift to a non-bipolar disorder at least once over the course of the 10 year study. Childhood psychopathology and poorer illness course were among the few variables associated with an increased odds of a change in diagnosis.

Conclusions—Even with optimal assessment practices, misdiagnosis of bipolar disorder is common, with complex clinical presentations often making it difficult to consistently diagnosis the disorder over the long-term.

Keywords

bipolar disorder; diagnosis; assessment; psychosis; prospective; validity; first-admission sample; mania; childhood behavior problems

INTRODUCTION

The long-term consistency of a psychiatric diagnosis is an essential criterion for establishing validity (1). Moreover, changes in diagnosis have serious implications for treatment. Both reasons make it important to understand the course of a diagnosis over time, as well as factors that lead to diagnostic changes. Among psychotic disorders, the diagnostic

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consistency of schizophrenia has been studied most (2). In contrast, fewer studies have focused on the extent to which patients with bipolar disorder maintain their diagnosis over the long term.

The largest, most closely followed sample of adults with bipolar disorder, the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression, reported the percent of depressed patients who developed mania and hypomania, the percent of hypomanic patients who developed mania, and the percent of patients with psychosis whose subsequent episodes also included psychosis (3–5). To our knowledge, however, the study did not consider diagnostic switching away from bipolar disorder to a non-bipolar diagnosis, making it impossible to determine the stability of the diagnosis over time.

Other studies have looked at this issue prospectively, but have limitations. In addition to relatively short follow-up periods (i.e., less than 3 years) (6–11), these studies had small samples sizes ranging from 14 to 30 (8, 12–16) or relied on case registries where diagnostic practices were not standardized (17–19). Finally, most did not follow samples early in their course of illness. With these caveats in mind, the diagnostic consistency of bipolar disorder in these samples, as measured by the percent of patients retaining this diagnosis from one assessment to the next, ranged from 49% to 91% (median = 70.0%, interquartile range = 50% to 83%) (8–12, 14, 16–18, 20–22), with two small studies (< 21 patients) and less rigorous methods showing wider variation (13, 15).

Beyond providing estimates of consistency, very few of the studies cited above examined factors that predicted whether a person's diagnosis was likely to change. The studies that did consider such factors found that both demographic (i.e., female, African-American race, and older age) and clinical variables (i.e., assessed in outpatient settings; number of assessments; being unmedicated; having psychotic symptoms or comorbid substance abuse) were associated with greater changes in diagnosis over time (9, 17, 22). Moreover, few of those studies enumerated alternative diagnoses.

Broadly speaking, two factors may lead to inconsistent diagnoses among patients followed over several years. The first involves changes in the course of the underlying psychopathology. For example, a patient previously diagnosed with major depressive disorder may develop a first episode of mania and therefore have a diagnostic change to bipolar disorder or a patient with bipolar disorder may develop a subsequent course more consistent with schizoaffective disorder. The second source of instability involves assessment error, broadly conceived. For example, clinicians may not consistently inquire about past manic symptoms (23) or patients may not recall them (24). Even using optimal assessment practices, a complicated clinical presentation, such as the presence of psychotic symptoms or a more severe course of illness, may make it difficult to accurately detect bipolar disorder, resulting in increased odds of misdiagnosis over time.

Beyond these variables, no study has ever considered the role that childhood factors may play in the consistency of a bipolar diagnosis in adulthood. At least three childhood variables may be especially important in this respect. First, childhood psychopathologies, particularly externalizing disorders, are associated with a worse course and increased comorbidity, such as substance abuse (25, 26) and antisocial behaviors, in adolescence and adulthood (27 for a review). As a result, such patients may present with a more complex clinical picture during assessment as adults, which in turn may lead to greater diagnostic instability. Second, childhood and adolescent onset of bipolar disorder, versus later age of onset, has also been associated with more complex psychopathology and poorer outcomes (28), which could similarly lead to more diagnostic confusion upon assessment. Third, premorbid adjustment is a strong predictor of illness course in schizophrenia (14). Thus,

poor social/school adjustment in childhood may be associated with diagnostic inconsistency later because these patients may have been diagnosed with bipolar disorder when in fact they have a schizophrenia-related disorder.

The present study had two goals. First, we sought to estimate the 10-year consistency of a bipolar diagnosis in a cohort identified at the time of their first psychiatric hospitalization. We hypothesized that the rate of diagnostic consistency would be high given that diagnoses were made based on best estimate methods, described in more detail below.

Second, we explored factors associated with the consistency or inconsistency of a bipolar diagnosis over time, a question rarely addressed by previous reports. We investigated demographic characteristics and clinical features (including illness course, treatment history and family psychiatric history). We also considered the effect of childhood factors on diagnostic consistency in adulthood. Insofar as respondents with higher rates of psychotic symptoms, poor premorbid adjustment, childhood psychopathology, substance abuse and antisocial behavior would present with more complex clinical pictures, we hypothesized that they would be given a bipolar diagnosis inconsistently, relative to respondents without these historical features. We explored these hypotheses in a clinical cohort with psychotic symptoms who were recruited from multiple inpatient facilities early in the course of illness and then followed for 10 years. Diagnoses were reconsidered at four time points. This study focuses on individuals who were diagnosed with bipolar disorder on at least one of these occasions. For those times when bipolar disorder was not given, we surveyed the common alternative diagnoses. Given that the cohort was initially recruited based on evidence of psychotic symptoms, we hypothesized that the most common alternative diagnosis among respondents initially diagnosed with bipolar disorder would be schizoaffective disorder.

METHOD

Sample and Procedures

The present report is based on a subsample of the Suffolk County Mental Health Project cohort, described in detail elsewhere (11, 29–31). Briefly, the cohort was recruited between 1989 and 1995 from the 12 psychiatric inpatient units of Suffolk County, New York. The facilities included community hospitals, a Veterans Administration hospital, a university hospital and state adult and children's hospitals. All patients who showed evidence of psychosis and who presented at one of these facilities were asked to participate in this study. Inclusion criteria were first admission to a psychiatric hospital within 6 months of enrollment into this study, age between 15 and 60, residency in Suffolk County, capacity to provide written informed consent, and clinical evidence of definite or possible psychosis. Potential participants were excluded if there was evidence of moderate to severe retardation or if they could not speak English. The procedures for obtaining informed consent were approved annually by the Institutional Review Boards at Stony Brook University and all hospitals where respondents were recruited.

A total of 628 participants met eligibility criteria and were assessed at baseline. Participants were interviewed by trained masters-level mental health professionals (primarily psychiatric social workers), usually 1–3 weeks after admission. Response rate for enrollment was 72%. Face-to-face follow-up interviews were conducted 6-months and 2 years later using the Structured Clinical Interview for DSM-III-R (32). A 10-year follow-up assessment was carried out using the psychosis and mood disorder modules of the SCID for DSM-IV. Systematic efforts were also made to collect collateral information. Specifically, at each assessment, participants were asked to identify an informant who was then interviewed either by phone or in person in order to collect information regarding the participant's symptoms. The interviewers received extensive training, and inter-rater reliability was

maintained over time by having the project director randomly observe and rate 5–10% of the interviews. The kappa for psychotic symptoms ranged from .81–1.0, while the kappa for negative symptoms ranged from .57 to 1.0. Ratings for mood symptoms had an average kappa of 0.73, based on 22 interviews.

The subsample used for the present study consisted of members of the larger cohort who received a DSM-IV research diagnosis of bipolar I (99.0%) or II (1.0%) disorder at any of the assessment waves and who had been interviewed on at least two occasions. Specifically, the analyses here focus on the 195 first-admission patients who had originally presented for treatment with evidence of psychosis and were then diagnosed with bipolar disorder on at least one occasion by the consensus assessment (described more below) between baseline and 10-year follow-up.

Best-estimate research diagnoses were made by consensus of the project's clinical psychiatrists on a case-by-case basis after review of all available information, including ratings from structured clinical interviews, interviewers' written narratives, medical records, information from significant others and school records. Best-estimate DSM-III-R diagnoses were assigned after the baseline interview, and best estimate DSM-IV diagnoses were assigned after the 6-month, 2-year and 10-year assessments (7, 11). The consensus team was blind to previous research consensus diagnoses.

Measures

Demographic, clinical, childhood and psychosocial functioning measures were examined in relation to diagnostic consistency. Demographic variables included sex, race (African American vs. other) and the following variables at baseline: education (whether they finished high school); marital status (never vs. ever married); employment status (full-time employed, student, or homemaker vs. other) and social class of household (white collar vs. blue collar or public assistance).

Several clinical variables were investigated including whether the initial bipolar diagnosis specified an episode of mania, versus a depressed or mixed state and whether the person was ever diagnosed with a mixed episode. Comorbid conditions included lifetime DSM-III-R drug and alcohol abuse and anxiety disorders (i.e., panic disorder, social phobia, OCD, and PTSD) measured as part of the SCID. Antisocial behavior was measured by history of incarceration and determined from the SCID overview and the demographics and life events modules created for the study (33). Psychosis severity included the average number of Schneiderian first rank symptoms, and severity of positive and negative symptoms measured with the Scale for the Assessment of Positive Symptoms (SAPS) (34) and the Scale for the Assessment of Negative Symptoms (SANS) (35). Symptomatic functioning was assessed using the Brief Psychiatric Rating Scale (BPRS) clinical global rating (36). Treatment variables included length of first hospitalization, type of hospital (i.e., public versus a community or private hospital), treatment with antidepressants or lithium prior to hospitalization, and whether the patient was diagnosed by the treating physician at the hospital with bipolar disorder. Family psychiatric history information was obtained from medical records and interviews with respondents and relatives at 6 months and 2 years modeled on Family History-Research Diagnostic Criteria (37). Family diagnoses of bipolar disorder, schizophrenia or any Axis I disorder were considered.

Childhood variables included the Cannon-Spoor Premorbid Adjustment Scale (average social and school functioning at ages 5–11, 12–15, and 16–18 years) (38), the age of onset of first diagnosable affective episode (before age 20 vs. later), and the presence of psychopathology during childhood. The latter two variables were determined from SCID histories, school and medical records, and interviews with significant others. Additional

information on ADHD, oppositional defiant and conduct disorders was obtained from the Child and Adolescent Symptom Inventory (39) and completed by 77% of the sample. A consensus childhood psychopathology variable (present or possible vs. no evidence) was derived from the aforementioned information (25) ($\kappa=0.88$ for categorization of child psychopathology versus no psychopathology for 20% of subjects, $n=40$).

Functioning over the course of the study was assessed with the Global Assessment of Functioning (GAF) ratings. GAF scores were given for the best month of functioning in the past year at baseline and in the interval during the follow-up.

Analysis Plan

Initial analyses focused on estimating the consistency of the bipolar diagnosis. Three measures of long-term diagnostic consistency were calculated (11). Prospective consistency was the proportion of people who were diagnosed with bipolar disorder at the baseline research assessment and retained the bipolar diagnosis at the 10 year assessment. Retrospective consistency was the proportion of people diagnosed with bipolar disorder at the final 10-year research assessment and who had this diagnosis at baseline.

Since there were four opportunities for consensus diagnosis, with some individuals only diagnosed with bipolar disorder during the interval between baseline and 10 years, we calculated the overall rate of consistency by taking the number of respondents who were diagnosed with bipolar disorder at every available assessment and dividing it by the entire sample of respondents who were diagnosed at least once with bipolar disorder.

Next, we stratified the sample into those who were consistently diagnosed with bipolar disorder at all available assessments and those who were inconsistently diagnosed across time. Respondents who dropped out or had missing assessments were considered “consistently diagnosed” if they were given a bipolar diagnosis at all of their available assessments. After stratifying the sample, we surveyed alternative primary diagnoses among the inconsistently diagnosed group.

To explore factors associated with diagnostic consistency, we compared participants with consistent versus inconsistent bipolar diagnoses on the demographic, clinical, childhood and illness course variables described above using *t*-tests and *chi-square* tests.

RESULTS

A total of 195 respondents with at least one follow-up were diagnosed by consensus with bipolar disorder at baseline, 6 months, 2 years and/or 10 year follow-up. Overall retention across the 10 years was high: 93.8% ($n = 183$) of participants completed at least three out of the four assessments and 77.9 % ($n = 152$) were rediagnosed at the 10 year wave. Furthermore, those who dropped out by year 10 were neither more nor less likely to have a change in diagnosis before then compared to those who completed the entire study, ($OR=0.7$, $OR\ CI = 0.4-1.4$, $\chi^2 = 1.0$, ns). Bipolar I disorder (versus Bipolar II) was diagnosed in 193 respondents.

10-Year Overall, Prospective, and Retrospective Consistency

Among the 195 respondents ever diagnosed with bipolar disorder in the study, 72.3% were given the diagnosis at baseline (141/195), 79.5% at 6 months (147/185 available at 6-months), 74.7% at 2 years (142/190 available at 2-years) and 75.2% at year 10 (115/153 available at year 10). Among all 195 respondents who at one point or another were diagnosed with bipolar disorder, only 98 (50.3%) were consistently diagnosed with the disorder at every available assessment. The other 97 respondents (49.7%) were

inconsistently diagnosed, having been given a non-bipolar diagnosis at least once in the course of 10 years.

The 10 year prospective consistency among respondents who were assessed at baseline and again at year 10 was 79.6 % (i.e., of 108 respondents who were diagnosed with bipolar disorder at baseline and reassessed at year 10, 86 retained a bipolar diagnosis at the 10 year follow-up). Conversely, the long-term retrospective consistency was 74.8% (i.e., 115 participants were diagnosed with bipolar disorder at year 10, among whom 86 had been given the same diagnosis at baseline).

Survey of Alternative Diagnoses in the Inconsistently Diagnosed Group

Among the 97 inconsistently diagnosed respondents, alternative diagnoses varied. Table 1 provides brief illustrative vignettes of cases that were inconsistently diagnosed, and Figure 1 displays the frequencies of alternative diagnoses at the different assessments. As seen in Figure 1, the most common non-bipolar diagnosis was a schizophrenia spectrum disorder (i.e., aggregating across all assessment periods, 52.4% of these alternative schizophrenia spectrum diagnoses were schizoaffective disorder, while 38.1% were schizophrenia and 9.5% were schizophreniform diagnoses).

Respondents who were inconsistently diagnosed followed different trajectories with respect to when and how they were given a bipolar diagnosis, as shown in Figure 2. One group ($n = 34$) began with a non-bipolar primary diagnosis, but ended up with a bipolar diagnosis by their final assessment. As noted above, a portion of this first group ($n = 8$) was originally diagnosed with major depressive disorder but switched to a bipolar diagnosis at some time during their 10 year course. The other common scenario ($n = 10$) among this first group of respondents was to start with an unclear diagnosis.

A second group ($n = 32$) of the inconsistently diagnosed respondents had the opposite pattern: they were initially given a bipolar diagnosis, but by their last assessment they had been switched to another primary diagnosis. The majority of them ($n = 18$) ended with their final assessment reflecting a schizophrenia spectrum disorder (8 with schizophrenia and 10 with schizoaffective disorder).

The third and final group ($n = 31$) had a random diagnostic pattern, with diagnoses switching to and from bipolar disorder at various time points with no clear pattern. No single alternative disorder clearly predominated in this group, although the majority ($n = 21$) were given a psychotic disorder at some point, with most of these ($n = 13$) being a schizophrenia spectrum disorder. Many of these respondents ($n = 11$) were also given an “unknown” diagnosis at some point as well.

Differences between Consistently and Inconsistently Diagnosed Respondents

Table 2 compares the consistently and inconsistently diagnosed groups on demographic and clinical characteristics. Participants who were consistently diagnosed were more likely to have been given a diagnosis of bipolar disorder at discharge from the hospital after their initial admission and to have initially had a manic episode (rather than a mixed or depressed episode). At baseline, inconsistently diagnosed respondents had a greater number of Schneiderian first rank psychotic symptoms, more serious overall symptoms as measured by the BPRS, and worse overall functioning as measured by the GAF. They were also more likely to have been incarcerated. Consistently diagnosed individuals were more likely to have been treated with lithium as expected from their discharge diagnosis. The groups did not differ with respect to rates of mixed episodes, comorbidity of anxiety or substance use disorders, type or intensity of treatment exposure, or family psychiatric history, including family history of bipolar disorder.

Table 3 compares the groups on childhood variables. Childhood psychopathology was significantly more frequent among the inconsistently diagnosed respondents (84.4% vs. 66.3% in the consistently diagnosed group), with 60.2% having had significant and impairing behavior disorder symptoms (i.e., attention deficit hyperactivity and/or conduct disorder and/or very early substance abuse) by age 15. As measured by the Cannon-Spoor Social Adjustment Scale, those with inconsistent bipolar diagnoses had worse premorbid functioning in elementary school (see table 3). Differences became more prominent by early adolescence (table 3). There was no significant difference in diagnostic consistency between those with an early versus older age of onset.

Table 4 shows differences between groups during the follow-up period. Across almost all periods, inconsistently diagnosed respondents tended to have worse functioning as measured by the GAF and were more symptomatic as measured by the BPRS, SANS and SAPS.

DISCUSSION

The present report estimated the long-term (i.e. 10-year) consistency of a bipolar diagnosis among first-admission respondents hospitalized with psychosis early in the course of their illness. It represents one of the first studies to examine multiple factors, particularly childhood factors, that could help explain lack of consistency in the bipolar diagnosis across time. The major findings indicated that among respondents who were diagnosed at least once with bipolar disorder across a 10 year period, only half (50.3%) were consistently given this diagnosis at every available assessment. Correlates of inconsistency included greater number of psychiatric symptoms, more psychotic symptoms, worse overall functioning, and presenting after a depressive or mixed episode versus a manic one. Childhood factors associated with diagnostic inconsistency included childhood psychopathology and worse premorbid functioning in adolescence.

The results can be understood in two ways. On the one hand, almost 80% of the cohort diagnosed at baseline with bipolar disorder retained this diagnosis at the 10 year follow-up, indicating that many cases of bipolar disorder can be reliably diagnosed from an early point in treatment. These estimates of prospective consistency are higher than those found in other studies (8, 9, 12, 14, 17, 18, 21, 22), highlighting how a comprehensive assessment relying on multiple sources of information can reduce diagnostic uncertainty.

On the other hand, only half of the respondents (50.3%) who were ever diagnosed with bipolar disorder were consistently given this diagnosis across the 10 years, that is received the diagnosis at every assessment. So while many respondents have a clear presentation with little diagnostic ambiguity, almost half are diagnostically confusing at some point, even in a research setting where diagnostic practices are more comprehensive than those in routine clinical care. Such a proportion is not insignificant, raising the question of what led to this uncertainty.

One explanation may be that some respondents initially manifested affective symptoms with psychosis but suffered from a different illness. The latter only became clearer over time as their symptoms evolved, with psychotic symptoms becoming more temporally prominent and their functioning declining markedly. This appears to have been the case for at least a third of the inconsistently diagnosed respondents (e.g., cases 4–5 in table 1). Many of them were initially diagnosed with bipolar disorder, but over the course of 10 years, their features had become more consistent with the diagnosis of a schizoaffective disorder or schizophrenia. Some may argue that some of these respondents, particularly those with schizoaffective disorder, manic subtype, are part of the bipolar spectrum (40) and therefore not different from those who were more consistently diagnosed. This is a theoretical issue,

but it is important to note that in the present sample, respondents who were given a schizoaffective diagnosis had developed clear symptoms of schizophrenia, though there remained occasional episodes of mania or depression superimposed. The development of negative symptoms and increased prominence of psychotic symptoms were also reflected in their lowered functioning over the follow-up. Therefore, this was not simply a poorer bipolar outcome group but the development of a different condition from bipolar disorder.

A second explanation for the diagnostic uncertainty among the inconsistently diagnosed respondents was that they had not yet manifested clear signs of bipolar disorder at baseline, resulting in a diagnostic shift later in the study. Indeed, many of the latter group were initially diagnosed with major depressive disorder or had an unknown diagnosis; most of these individuals were re-diagnosed with bipolar disorder because their symptom picture had changed or become clearer (e.g., cases 1–3 in table 1). These findings highlight the need for early diagnoses among patients originally presenting with psychosis to be conceptualized as provisional until the course of the disorder makes the diagnosis clearer. While data specifically pertaining to MDD with psychosis are not the focus of the present report, it is important to note that most people with this diagnosis did not go on to develop bipolar disorder (11).

This left about 16% of the sample with a random diagnostic pattern that could not be easily grouped. They demonstrated a complex interplay of developmental, behavioral, substance abuse and clinical symptoms that made mania and depression criteria difficult to apply and interpret consistently.

In comparing respondents who were inconsistently diagnosed with bipolar disorder to those who were consistently diagnosed, we found that the latter group was more likely to have had a manic episode and to have been identified by their treating physician as having bipolar disorder at the time of their initial admission. This again suggests that for many respondents, a correct diagnosis is obvious at early stages of treatment. Conversely, respondents with an unstable diagnostic picture tended to have more complex psychiatric symptoms, including a greater number of psychotic symptoms, which most likely reflected the confusion between schizophrenia spectrum disorder and bipolar disorder.

With respect to childhood factors, respondents with evidence of childhood psychopathology and poorer premorbid functioning beginning in early adolescence were much more likely to be inconsistently diagnosed. How these childhood variables affected the diagnostic picture is not entirely clear. Part of their effects on diagnosis may be mediated by worse global functioning prior to the initial baseline assessment, which may have led to a more complex clinical presentation. Alternatively, childhood behavior problems may have represented early manifestations of schizophrenia; indeed, behavior problems and poor premorbid adjustment are known to be associated with schizophrenia outcomes (41–43). If so, some of these respondents may have had a schizophrenia spectrum disorder that was confused with bipolar disorder initially, resulting in inconsistent diagnoses in adulthood.

Other variables that we hypothesized would distinguish between consistently and inconsistently diagnosed respondents were non-significant, including the presence of mixed symptoms at times other than the initial presentation. Substance abuse was common in the entire sample but was not associated with more diagnostic inconsistency. Its severity was not analyzed for this report, however, and future studies might consider whether severity of substance abuse is a distinguishing factor.

Findings may also have implications for the validity of our current psychiatric nosology as well for diagnostic guidelines for patients hospitalized with psychotic symptoms. Clearly, a large subset of patients have a stable diagnostic course over time, suggesting that our bipolar

I disorder construct is valid (at least with regard to course). However, an equally large number of patients had an unstable diagnostic path. For many patients, diagnostic uncertainty diminished over the follow-up. These findings suggest that, short of presenting with an uncomplicated manic episode, longitudinal clarification of symptoms may be necessary before confidently establishing a bipolar diagnosis at least among patients whose initial hospitalization involves psychosis. Given that comorbidity with childhood-onset behavior disorders occurred more frequently in participants with unstable diagnoses, circumspection for their diagnosis might be especially warranted.

Findings from this study must be viewed within the context of its limitations. Among these, results are based on a group of primarily bipolar I manic patients initially hospitalized with psychosis, which may limit generalizability. This limitation is offset in part by significant benefits of this recruitment approach: Salvatore and colleagues (44) note that first-episode follow-up studies like the current one are less likely to be confounded by the effects of recruiting from settings where patients may be in later stages of their illness. As a result, the current sample is less likely to be confounded by the effects of chronic illness, disability, institutionalization, and changes produced from years of treatment (44). The analysis was also limited by the presence of some missing data, as well as the fact that the impact of Axis II psychopathology was not considered. The missing data limitation was mitigated by two factors. First, attrition was remarkably small for a study of this length. Second, missingness was not related to our primary outcomes, providing no evidence that dropping out was related to the consistency or inconsistency of a bipolar diagnosis. Lastly, although the clinicians responsible for consensus diagnosis were blind to previous research diagnoses, interviewers performing the SCID interviews were aware of prior SCID diagnoses. We would suggest, however, that this would lead to greater diagnostic consistency rather than the pattern found here.

In summary, in one of the longest studies to ever follow people with bipolar disorder, the diagnosis was found to be highly variable. Half were consistently given the diagnosis across a 10-year period involving four research assessments. Yet for the other half, the phenomenology was not sufficiently clear to provide long-term diagnostic consistency even when using state of the art assessments and expert diagnosticians. Several studies have noted that a number of years elapse before the correct diagnosis of bipolar disorder is made, with some suggesting that part of the reason for the delay may be a neglect to carefully screen for bipolar disorder (e.g., 45). The present study makes clear that even with optimal assessment practices, diagnosing bipolar disorder early and consistently over the long-term remains a major challenge.

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Figure 1.
Frequency of Diagnoses Among the Inconsistently Diagnosed Group (N = 97)

Figure 2.
Diagnostic Trajectories Across 10 Years Among Respondents Who Were Diagnosed at Least Once With Bipolar Disorder (N = 195)

Table 1**Case Examples Illustrating Childhood Psychopathology and Diagnostic Inconsistency**

Initially non-bipolar diagnosis, but ended with a bipolar diagnosis	
1	Some ADHD symptoms in childhood but decent student until he started drinking; initially diagnosed with major depressive disorder with psychosis following many stressors and a severe drinking spree; clear mixed episode 12 months later; some question whether first episode was, in fact, mixed; bipolar I disorder diagnosis at year 10.
2	Suffered physical abuse as a child and into adulthood; experienced severe anxiety with panic; reported a history of stimulant abuse; very bizarre at admission and called schizophreniform; subsequent course was relapsing and remitting; episodes appeared more clearly manic and depressed over time with a bipolar I diagnosis by year 10.
3	Attended special education in childhood; IQ score of 76; described chaotic life; diagnosed with post partum depression with psychosis at age 20; followed a rapid cycling course thereafter and diagnosed with bipolar I disorder at year 10.
Initially diagnosed with bipolar disorder, but ended with another diagnosis	
4	Physically abused in childhood; diagnosed with ADHD with impairment; violent and disruptive as child; dropped out of school in 10 th grade; index episode-severe psychosis with thought broadcasting possibly following paroxetine; denied affective symptoms but "significant other" described manic symptoms; subsequent depression; in remission at year 2; by year 4 had mild ideas of reference and mild cycles in spite of treatment but working full time; by year 10, does little, isolated, can't work and chronically delusional without mood symptoms and in spite of treatment; diagnosed with schizoaffective disorder at year 10 but question of paranoid schizophrenia.
5	Denied childhood problems; college graduate; functioned well; at index episode, paranoid, anxious, activated, thought broadcasting; called manic with mood incongruent psychosis; followed by MDD but still psychotic and bizarre; cannabis dependence; treated; remitted at year 2; subsequently, more episodes characterized by fear and anxiety with psychosis; called "mixed" or possible MDD with psychosis; by year 10, chronically paranoid and delusional; hospitalizations for severe psychosis without mood symptoms; couldn't work any longer; relates only to family; 10 year diagnosis is schizophrenia, paranoid type.
Bipolar diagnosis given inconsistently	
6	Retained in kindergarten; special education through 9 th grade; IQ 90 but not great informant; index episode-sudden onset severe psychosis; called schizophreniform but many manic symptoms; functioned relatively well taking lithium; at 4 years appeared to have clear manic episode; over the next 6 years, developed chronic persecutory delusions; chronically unemployed; cared for by family; socializes only with family; some manic symptoms; diagnosed at year 10 with schizoaffective disorder.
7	Childhood anxiety; stormy adolescence (runaway; incarcerated for selling drugs); chronically odd; heavy THC use; index episode-LSD psychosis followed by several psychiatric hospitalizations; with what was called psychotic depression followed by manic symptoms; when remitted, functioning marginally though graduated from college. Called psychosis NOS; subsequently, mania with psychosis and continued drug abuse; at year 10, no psychosis, quite social, relying on relatives financially because he could; had been off cocaine for several months; given a bipolar I diagnosis with antisocial traits and poly substance abuse.
8	Born premature; on respirator for 8 months, called "slow"; also given ADHD diagnosis in childhood; index episode-psychotic and bizarre; called schizophreniform; at 6 months, depression followed by manic episode; drug-involved; antisocial behavior. At 10 years, psychosis and bizarre behavior with and without mood symptoms and with and without drug involvement; chronic and declining course; called schizoaffective, bipolar.

Table 2

Baseline Demographic and Clinical Characteristics of a First Admission Cohort Who Were Consistently and Inconsistently Diagnosed With Bipolar Disorder Over the Course of 10 Years (N = 195)

	Consistently Diagnosed ^a (n = 98)	Inconsistently Diagnosed ^b (n = 97)	OR or t	OR CI	p-value
Background characteristics					
Age at baseline, M (SD)	30.3 (10.4)	28.4 (10.0)	1.3	--	ns
Female, % (n)	56.1 (55)	43.3 (42)	0.6	0.3 – 1.1	ns
High school graduate, % (n)	88.7 (86)	84.5 (82)	0.7	0.3–1.6	ns
African American, % (n)	5.1 (5)	10.3 (10)	2.1	0.7–6.5	ns
Never married, % (n)	55.1 (54)	61.9 (60)	1.3	0.7 – 2.3	ns
Full-time employed, student, or homemaker, % (n)	56.3 (54)	45.4 (44)	0.6	0.4 – 1.1	ns
Household SES (White Collar), % (n)	59.7 (43)	56.9 (41)	1.1	0.6 – 2.2	ns
Baseline clinical variables					
Lifetime substance use diagnosis, % (n)	51.0 (50)	58.8 (57)	1.4	0.8 – 2.4	ns
Lifetime anxiety disorder, % (n)	48.0 (47)	52.6 (51)	1.2	0.7–2.1	ns
Incarcerated, % (n)	11.2 (11)	25.8 (25)	2.7	1.3–6.0	.01
Number of Schneiderian symptoms, M (SD)	0.4 (0.9)	0.8 (1.2)	–2.5	--	.01
GAF best in past year, M (SD)	68.8 (9.6)	63.9 (11.8)	3.2	--	.002
BPRS, M (SD)	38.0 (8.6)	41.0 (8.8)	–2.4	--	.02
SANS, M (SD)	0.8 (0.7)	1.1 (0.8)	–2.8	--	.006
SAPS, M (SD)	1.9 (0.8)	1.8 (1.0)	0.6	--	ns
Bipolar disorder characteristics					
Ever diagnosed with a mixed episode, % (n)	20.4 (20)	16.5 (16)	0.8	0.4 – 1.6	ns
First diagnosis of bipolar disorder included mania, % (n)	80.6 (79)	66.0 (64)	0.5	0.2 – 0.9	.02
Family history					
Family history of bipolar disorder, % (n)	19.5 (17)	13.5 (12)	0.6	0.3 – 1.4	ns
Family history of schizophrenia spectrum disorder, % (n)	7.1 (7)	7.2 (7)	1.0	0.3 – 3.0	ns
Family history of any disorder (excluding substance), % (n)	66.3 (65)	58.8 (57)	0.7	0.4 – 1.3	ns
Treatment History					

	Consistently Diagnosed ^a (n = 98)	Inconsistently Diagnosed ^b (n = 97)	OR or t	OR CI	p-value
Length of 1 st hospitalization, M (SD)	23.3 (26.3)	26.7 (38.1)	-0.7	--	ns
Type of Hospital - public (vs. community/private), % (n)	23.5 (23)	30.5 (29)	1.4	0.8 - 2.7	ns
Discharge diagnosis = bipolar, % (n)	68.4 (65)	40.7 (37)	0.3	0.2 - 0.6	<.001
Lifetime antidepressant use, % (n)	50.6 (43)	57.1 (48)	1.3	0.7 - 2.4	ns
Lifetime Lithium use, % (n)	73.3 (63)	58.3 (49)	0.5	0.3 - 1.0	.04

Note. Percentage denominators exclude missing data.

^a Respondents diagnosed with bipolar disorder at every completed assessment.

^b Respondents inconsistently diagnosed with bipolar disorder.

Table 3
Childhood Variables in Respondents Consistently or Inconsistently Diagnosed with Bipolar Disorder (N = 195)

	Consistently Diagnosed ^a (n = 98)	Inconsistently Diagnosed ^b (n = 97)	OR or t	OR CI	p-value
Illness onset before age 20, %(n)	25.5 (25)	29.9 (29)	1.2	0.7–2.4	ns
Childhood psychopathology, %(n)	66.3 (65)	84.4 (76)	2.8	1.4–5.6	.004
Childhood externalizing disorder, %(n)	20.4 (20)	54.6 (53)	4.7	2.5 – 8.9	<.001
Child and adolescent adjustment					
Age 5–11, M (SD) ^c	0.2 (0.2)	0.3 (0.2)	–1.9	--	.06
Age 12–15, M (SD) ^c	0.2 (0.2)	0.3 (0.2)	–2.0	--	.05
Age 16–18, M (SD) ^c	0.2 (0.2)	0.3 (0.2)	–3.1	--	.002

Note. Percentage denominators exclude missing data.

^a Respondents diagnosed with bipolar disorder at every completed assessment.

^b Respondents inconsistently diagnosed with bipolar disorder.

^c Higher scores indicate worse adjustment.

Table 4

Differences in Clinical Functioning During the Follow-Up (N = 195)

	Consistently Diagnosed ^a (n = 98)	Inconsistently Diagnosed ^b (n = 97)	t	p-value
6-Months	M (SD)	M (SD)		
GAF	67.2 (11.3)	61.7 (13.4)	2.9	.004
BPRS	24.3 (5.3)	27.0 (8.5)	-2.4	.02
SANS	0.7 (0.7)	0.8 (0.7)	-1.1	ns
SAPS	0.2 (0.3)	0.4 (0.7)	-3.2	.002
2-Year				
GAF	70.6 (9.6)	61.9 (13.1)	4.8	<.001
BPRS	25.2 (6.9)	28.0 (8.5)	-2.1	.03
SANS	0.5 (0.6)	1.0 (0.7)	-3.7	<.001
SAPS	0.3 (0.5)	0.5 (0.8)	-2.0	.049
10-Year				
GAF	69.9 (12.8)	62.2 (14.4)	3.4	.001
BPRS	24.1 (7.3)	28.2 (7.2)	-3.1	.002
SANS	0.3 (0.5)	0.9 (0.8)	-4.2	<.001
SAPS	0.2 (0.4)	0.5 (0.8)	-3.2	.002

Note.

^a Respondents diagnosed with bipolar disorder at every completed assessment.^b Respondents inconsistently diagnosed with bipolar disorder.